

Figure 1 Oligodeoxynucleotides Phosphorothioate and Site of Modification

Oligo No.	Sequence & Modification
8	5'-CCTACTAG <u>C</u> GTTCTCATC-3' (133-1)
9	5'-CCTACTAGC <u>X</u> TTCTCATC-3' (139-2)
10	5'-CCTACTAXCGTTCTCATC-3' (133-2)
11	5'-CCTACTX <u>G</u> CGTTCTCATC-3' (139-3)
12	5'-CCTAC <u>X</u> AGCGTTCTCATC-3' (133-3)
13	5'-CCTAXTAGCGTTCTCATC-3' (139-4)
14	5'-CCTXCTAGCGTTCTCATC-3' (133-4)
15	5'-CCTXCTAG <u>C</u> CTTCTCATC-3' (145-10a)
16	5'-CCTACTAGCGXTCTCATC-3' (133-5)
17	5'-CCTACTAGCGTXCTCATC-3' (139-7)
18	5'-CCTACTAGCGTTXTCATC-3' (133-6)
19	5'-CCTACTAGCGTTCXCATC-3' (139-8)
20	5'-CCTXXTAGCGTTCTCATC-3' (133-12)
21	5'-XXTACTAGCGTTCTCATC-3' (139-6)
22	5'-CCTACTAGCGTTCXXATC-3' (139-9)
23	5'-CCTXCTXCGTTCTCATC-3' (145-10b)

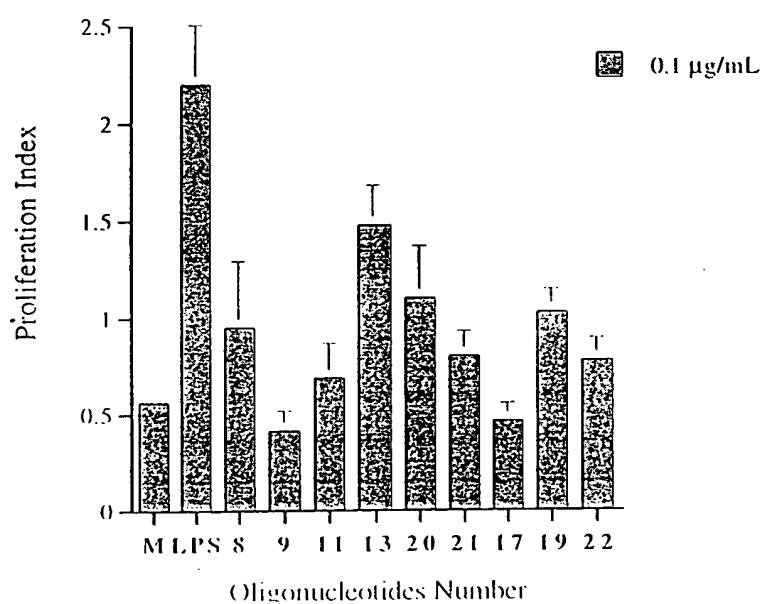
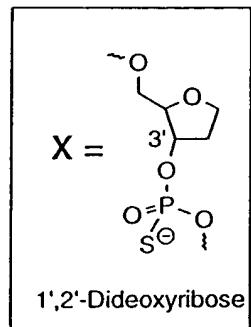


Figure 2 Oligodeoxynucleotides Phosphorothioate and Site of Modification

Oligo No.	Sequence & Modification
8	5'-CCTACTAG <u>C</u> GTTCTCATC-3' (133-1)
9	5'-CCTACTAGCXTTCTCATC-3' (139-2)
10	5'-CCTACTAXCGTTCTCATC-3' (133-2)
11	5'-CCTACTXGCGTTCTCATC-3' (139-3)
12	5'-CCTACXAGCGTTCTCATC-3' (133-3)
13	5'-CCTAXTAGCGTTCTCATC-3' (139-4)
14	5'-CCTXCTAGCGTTCTCATC-3' (133-4)
15	5'-CCTXCTAG <u>C</u> CTTCTCATC-3' (145-10a)
16	5'-CCTACTAGCGXTCTCATC-3' (133-5)
17	5'-CCTACTAGCGTXCTCATC-3' (139-7)
18	5'-CCTACTAGCGTTXTCATC-3' (133-6)
19	5'-CCTACTAGCGTTCXCATC-3' (139-8)
20	5'-CCTXXTAGCGTTCTCATC-3' (133-12)
21	5'-XXTACTAGCGTTCTCATC-3' (139-6)
22	5'-CCTACTAGCGTTCXXATC-3' (139-9)
23	5'-CCTXCTXGCGTTCTCATC-3' (145-10b)

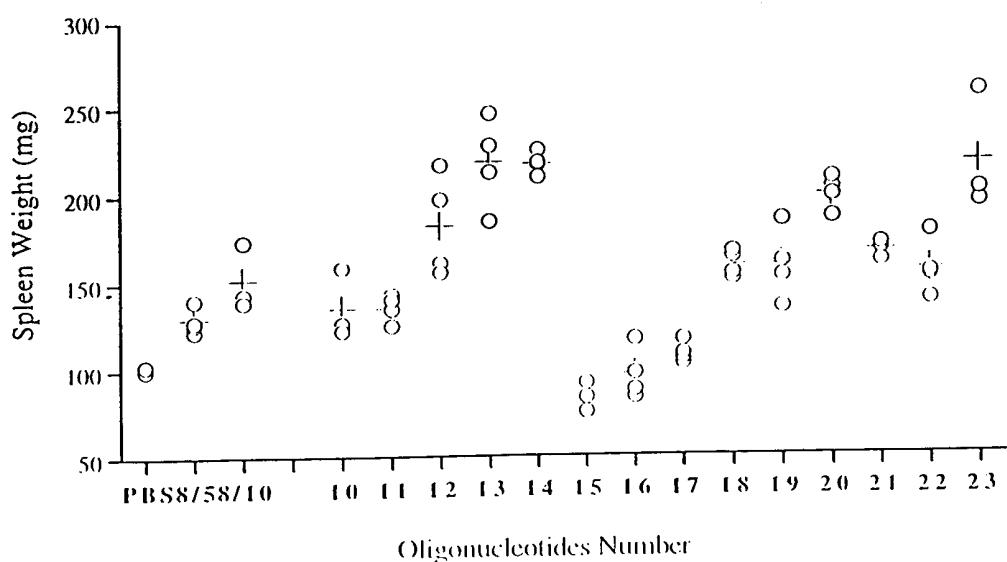
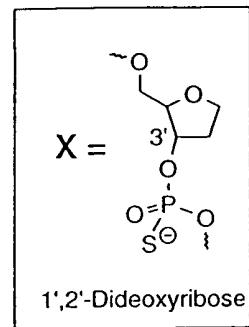
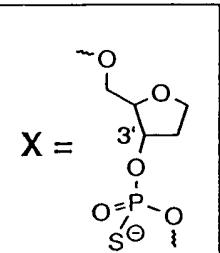


Figure 3 Oligodeoxynucleotides Phosphorothioate and Site of Modification

Oligo No.	Sequence & Modification
1	5'-CTATCTGAC <u>G</u> TTCCTCTGT-3' (131-1)
2	5'-CTATCTGAXGTTCTCTGT-3' (131-13)
3	5'-CTATCTGXCGTTCTCTGT-3' (131-2)
4	5'-CTATCXGACGTTCTCTGT-3' (131-3)
5	5'-CTAXCTGACGTTCTCTGT-3' (131-4)
6	5'-CTATCTGACGXCTCTGT-3' (131-5)
7	5'-CTATCTGACGTTCTCTGT-3' (131-6)

$X =$



1',2'-Dideoxyribose

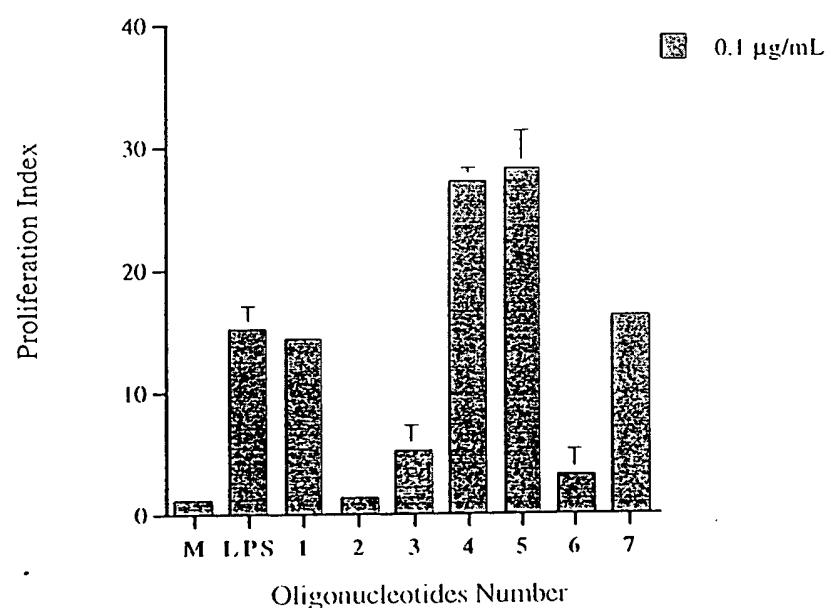


Figure 4 Oligodeoxynucleotides Phosphorothioate and Site of Modification

Oligo No.	Sequence & Modification
1	5'-CTATCTGAC <u>G</u> TTCCTGT-3' (131-1)
2	5'-CTATCTGAXGTTCTCTGT-3' (131-13)
3	5'-CTATCTGXCGTTCTCTGT-3' (131-2)
4	5'-CTATCXGACGTTCTCTGT-3' (131-3)
5	5'-CTAXCTGACGTTCTCTGT-3' (131-4)
6	5'-CTATCTGACGXTCCTGT-3' (131-5)
7	5'-CTATCTGACGTTXTCTGT-3' (131-6)

$X =$

1',2'-Dideoxyribose

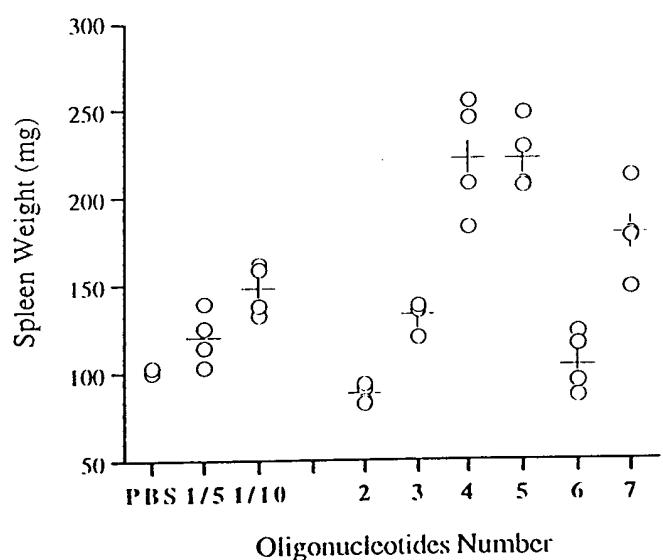


Figure 5 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification
133-1	5'-CCTACTAGCGTTCTCATC-3'
141-2	5'-CCTACTAGCXTTCTCATC-3'
141-3	5'-CCTACTXGCGTTCTCATC-3'
141-4	5'-CCTAXTAGCGTTCTCATC-3'
141-5	5'-CCTXXTAGCGTTCTCATC-3'
141-6	5'-XXTACTAGCGTTCTCATC-3'
141-7	5'-CCTACTAGCGTXCTCATC-3'
141-8	5'-CCTACTAGCGTTCXCATC-3'
141-9	5'-CCTACTAGCGTTXXATC-3'
131-1	5'-CTATCTGACGTTCTCTGT-3'
137-2	5'-CTATCTGXCAGTTCTCTGT-3'
137-3	5'-CTATCXGACGTTCTCTGT-3'
137-4	5'-CTAXCTGACGTTCTCTGT-3'

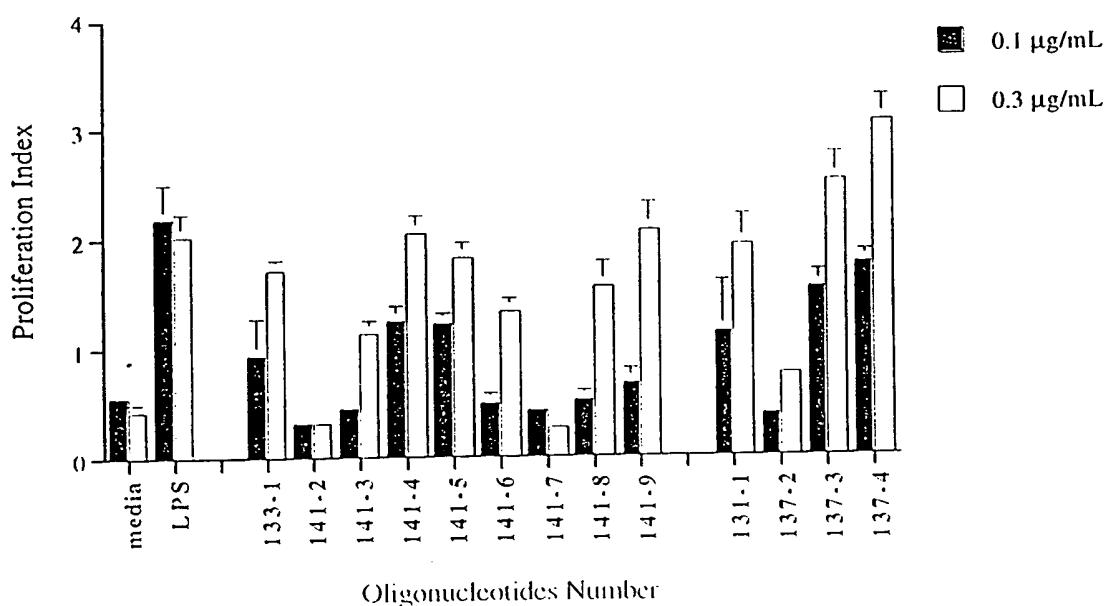
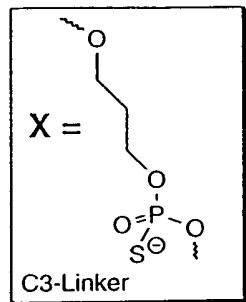


Figure 6 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification
133-1	5'-CCTACTAGCGTTCTCATC-3'
141-2	5'-CCTACTAGCXCTTCTCATC-3'
141-3	5'-CCTACTXCGTTCTCATC-3'
141-4	5'-CCTAXTAGCGTTCTCATC-3'
141-5	5'-CCTXXTAGCGTTCTCATC-3'
141-6	5'-XXTACTAGCGTTCTCATC-3'
141-7	5'-CCTACTAGCGTXCTCATC-3'
141-8	5'-CCTACTAGCGTTCXCATC-3'
141-9	5'-CCTACTAGCGTTCXXATC-3'
131-1	5'-CTATCTGACGTTCTCTGT-3'
137-2	5'-CTATCTGXCACGTTCTCTGT-3'
137-3	5'-CTATCXGACGTTCTCTGT-3'
137-4	5'-CTAXCTGACGTTCTCTGT-3'

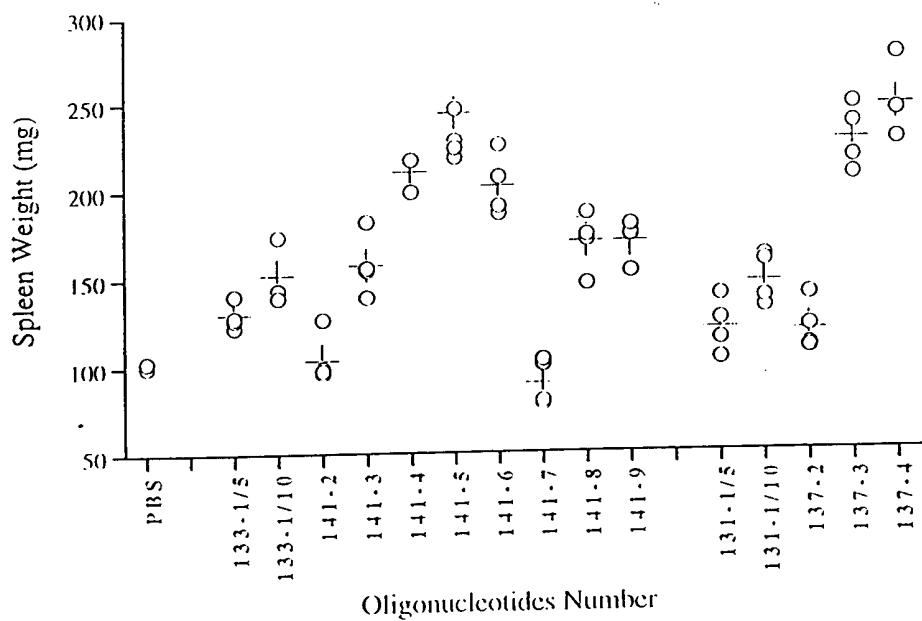
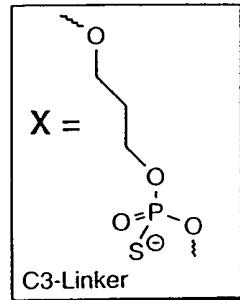
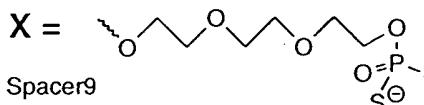
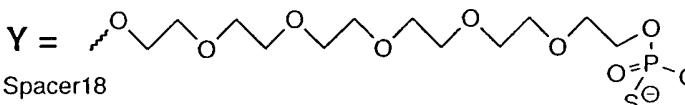


Figure 7 Oligodeoxynucleotides Phosphorothioate and Site of Modification

Oligo No.	Sequence & Modification
1	5'-CTATCTGAC <u>G</u> TTCCTGT-3' (131-1)
2	5'-CTAXCTGACGTTCTGT-3' (153-1)
3	5'-CTATCTGACGTT <u>C</u> XCTGT-3' (153-2)
4	5'-CTAYCTGACGTTCTGT-3' (153-3)
5	5'-CTATCTGACGTT <u>C</u> YCTGT-3' (153-4)
6	5'-CCTACTAGCGTTCTCATC-3' (133-1)
7	5'-CCTXCTAGCGTTCTCATC-3' (155-1)
8	5'-CCTACTAGCGTT <u>C</u> XCATC-3' (155-2)
9	5'-CCTYCTAGCGTTCTCATC-3' (155-3)
10	5'-CCTACTAGCGTT <u>C</u> YCATC-3' (155-4)

X = 
 Spacer9

Y = 
 Spacer18

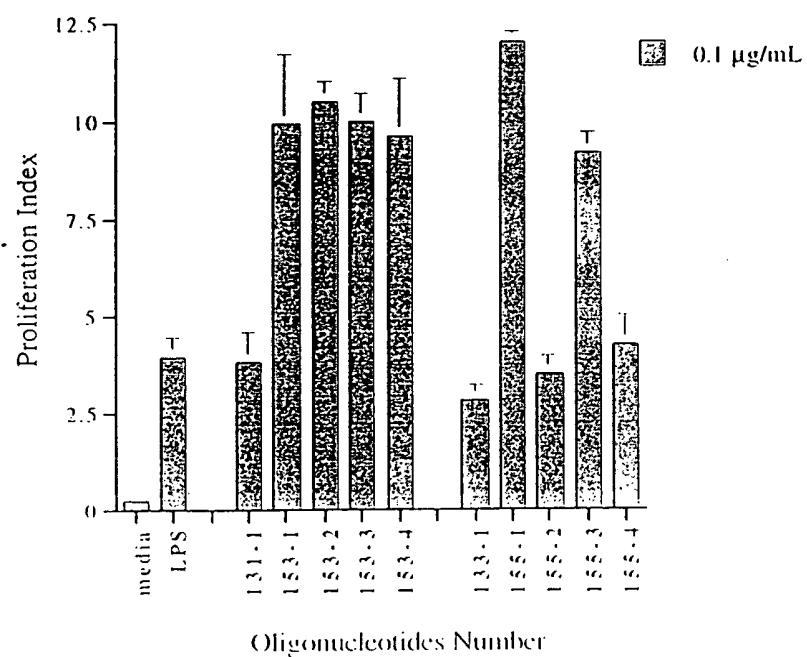
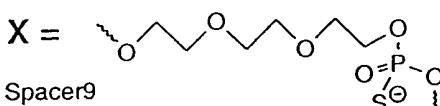
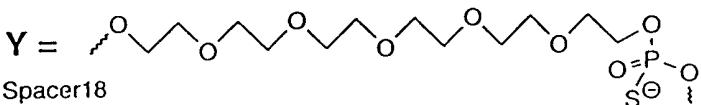


Figure 8 Oligodeoxynucleotides Phosphorothioate and Site of Modification

Oligo No.	Sequence & Modification
1	5'-CTATCTGAC <u>G</u> TTCCTGT-3' (131-1)
2	5'-CTAXCTGACGTTCTCTGT-3' (153-1)
3	5'-CTATCTGACGTT <u>C</u> XCTGT-3' (153-2)
4	5'-CTAYCTGACGTTCTCTGT-3' (153-3)
5	5'-CTATCTGACGTT <u>C</u> YCTGT-3' (153-4)
6	5'-CCTACTAGCGTTCTCATC-3' (133-1)
7	5'-CCTXCTAGCGTTCTCATC-3' (155-1)
8	5'-CCTACTAGCGTT <u>C</u> XCATC-3' (155-2)
9	5'-CCTYCTAGCGTTCTCATC-3' (155-3)
10	5'-CCTACTAGCGTT <u>C</u> YCATH-3' (155-4)

X = 
 Spacer9

Y = 
 Spacer18

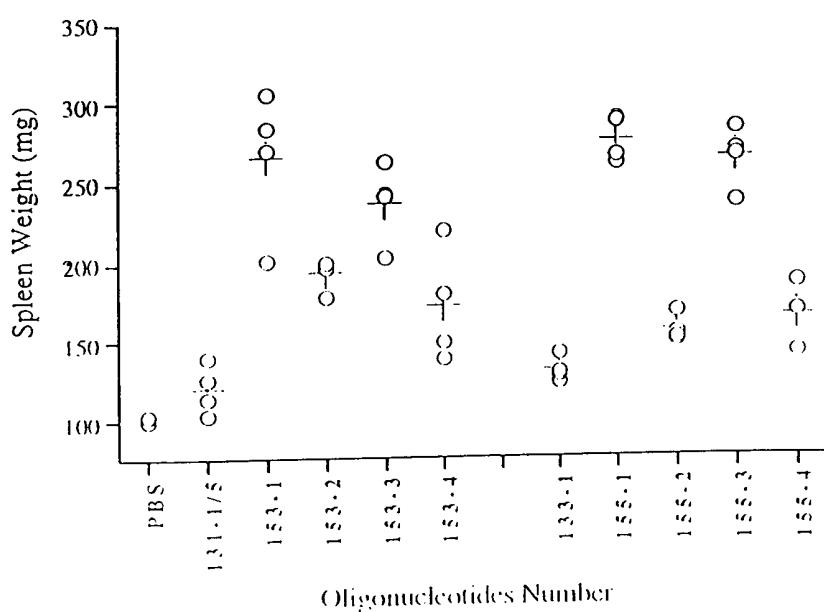


Figure 9 Oligodeoxynucleotides Phosphorothioate and Site of Modification

Oligo No.	Sequence & Modification
1	5'-CTATCTGACGTTCTCTGT-3' (131-1)
2	5'-CTATCTGXCAGTTCTCTGT-3' (157-1)
3	5'-CTATCTXACGTTCTCTGT-3' (157-2)
4	5'-CTAXCTGACGTTCTCTGT-3' (157-3)
5	5'-CTATCTGACGTXCTCTGT-3' (157-4)
6	5'-CTATCTGACGTTCXCTGT-3' (157-5)

X =

Amino-Linker

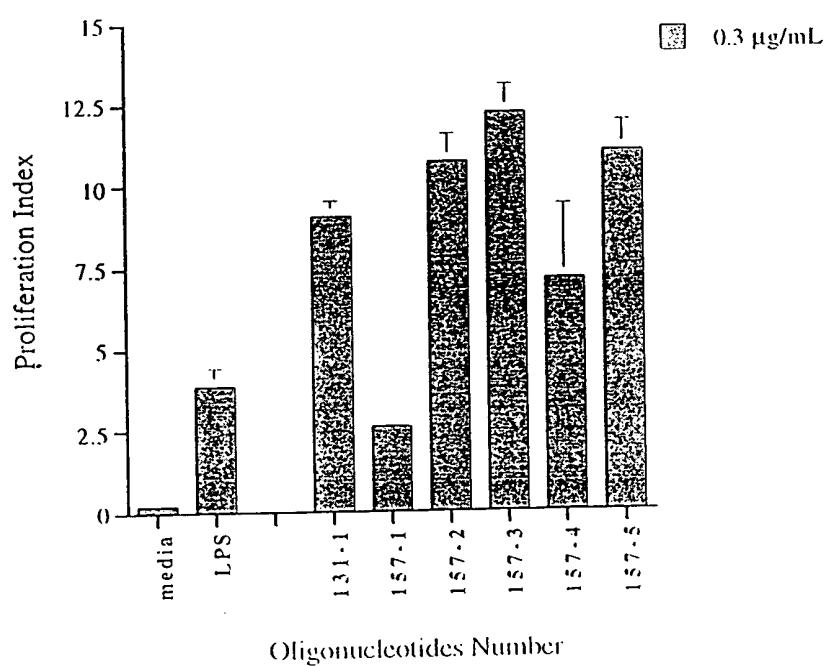


Figure 10 Oligodeoxynucleotides Phosphorothioate and Site of Modification

Oligo No.	Sequence & Modification
1	5'-CTATCTGACGTTCTCTGT-3' (131-1)
2	5'-CTATCTGXCAGTTCTCTGT-3' (157-1)
3	5'-CTATCTXACGTTCTCTGT-3' (157-2)
4	5'-CTAXCTGACGTTCTCTGT-3' (157-3)
5	5'-CTATCTGACGTXCTCTGT-3' (157-4)
6	5'-CTATCTGACGTTXCTGT-3' (157-5)

X =

Amino-Linker

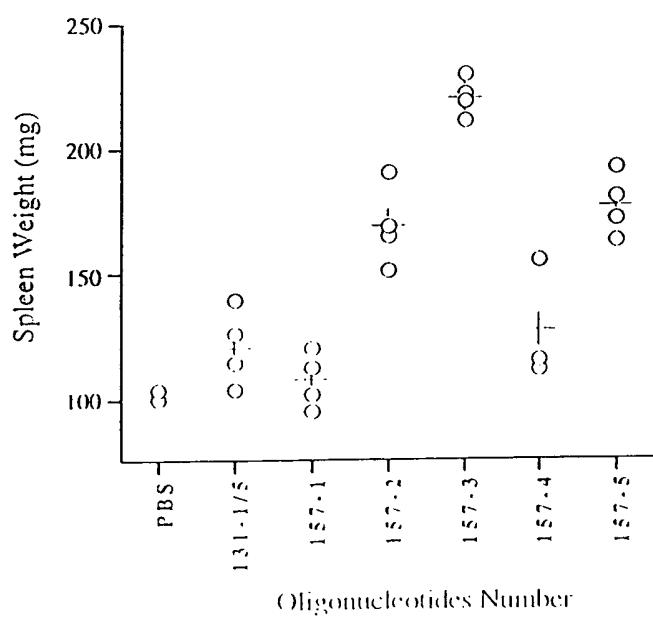
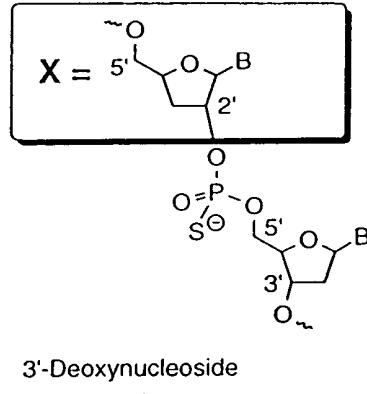


Figure 11 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification
131-1	5'-CTATCTGACGTTCTCTGT-3'
159-1	5'-CTATCTGACXTTCTCTGT-3'
159-2	5'-CTATCTGAXGTTCTCTGT-3'
159-3	5'-CTATXTGACGTTCTCTGT-3'
159-4	5'-CTATCTGACGTTCTXTGT-3'
133-1	5'-CCTACTAGCGTTCTCATC-3'
161-1	5'-CCTACTAGCXTTCTCATC-3'
161-2	5'-CCTACTAGXGTTCTCATC-3'
161-3	5'-CCTACTAXCGTTCTCATC-3'
161-4	5'-CCTAXTAGCGTTCTCATC-3'
161-5	5'-CCTACTAGCGTTCTXATC-3'



3'-Deoxynucleoside

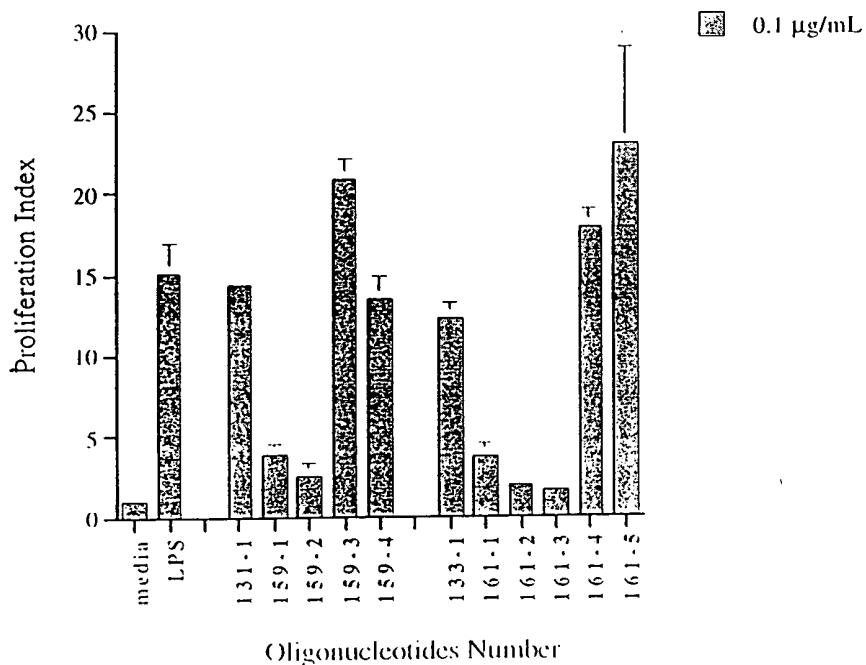
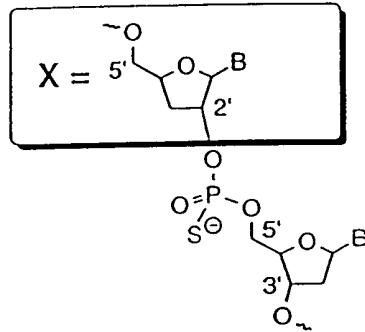


Figure 12 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification
131-1	5'-CTATCTGACGTTCTCTGT-3'
159-1	5'-CTATCTGACXTTCTCTGT-3'
159-2	5'-CTATCTGAXGTTCTCTGT-3'
159-3	5'-CTATXTGACGTTCTCTGT-3'
159-4	5'-CTATCTGACGTTCTXTGT-3'
133-1	5'-CCTACTAGCGTTCTCATC-3'
161-1	5'-CCTACTAGCXTTCTCATC-3'
161-2	5'-CCTACTAGXGTTCTCATC-3'
161-3	5'-CCTACTAXCGTTCTCATC-3'
161-4	5'-CCTAXTAGCGTTCTCATC-3'
161-5	5'-CCTACTAGCGTTCTXATC-3'



3'-Deoxynucleoside

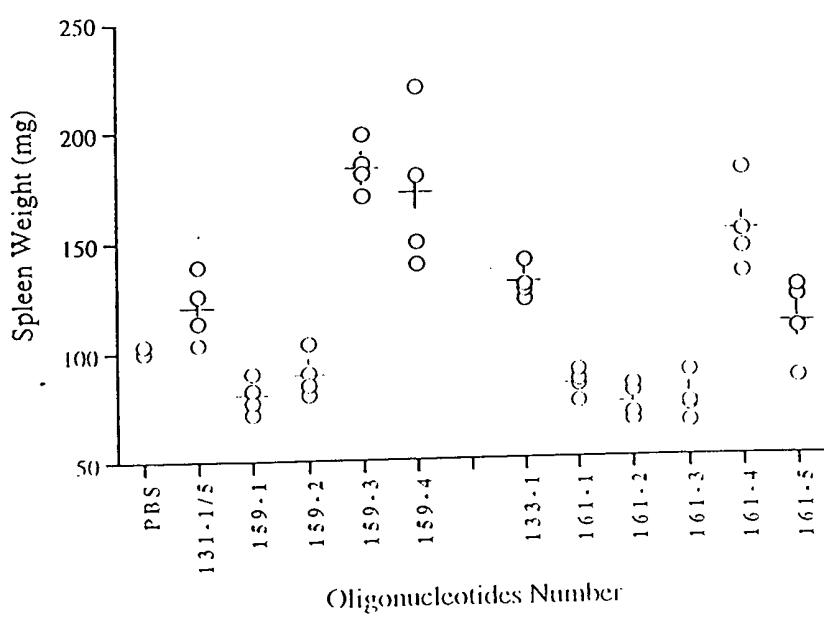
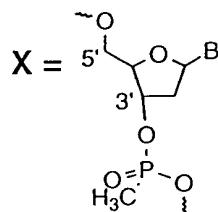


Figure 13 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification
131-1	5'-CTATCTGACGTTCTCTGT-3'
167-1	5'-CTATCTGXCAGTTCTCTGT-3'
167-2	5'-CTATCTXACGTTCTCTGT-3'
167-3	5'-CTATCXGACGTTCTCTGT-3'
167-4	5'-CTATXTGACGTTCTCTGT-3'
167-5	5'-CTAXCTGACGTTCTCTGT-3'
167-6	5'-CTXXCTGACGTTCTCTGT-3'
167-7	5'-CTATCTGACGXCTCTGT-3'
167-8	5'-CTATCTGACGTXCTCTGT-3'
167-9	5'-CTATCTGACGTTXTCTGT-3'
167-10	5'-CTATCTGACGTTXCTGT-3'
167-11	5'-CTATCTGACGTTCTXTGT-3'
167-12	5'-CTATCTGACGTTCTXXGT-3'



Methyl-phosphonate

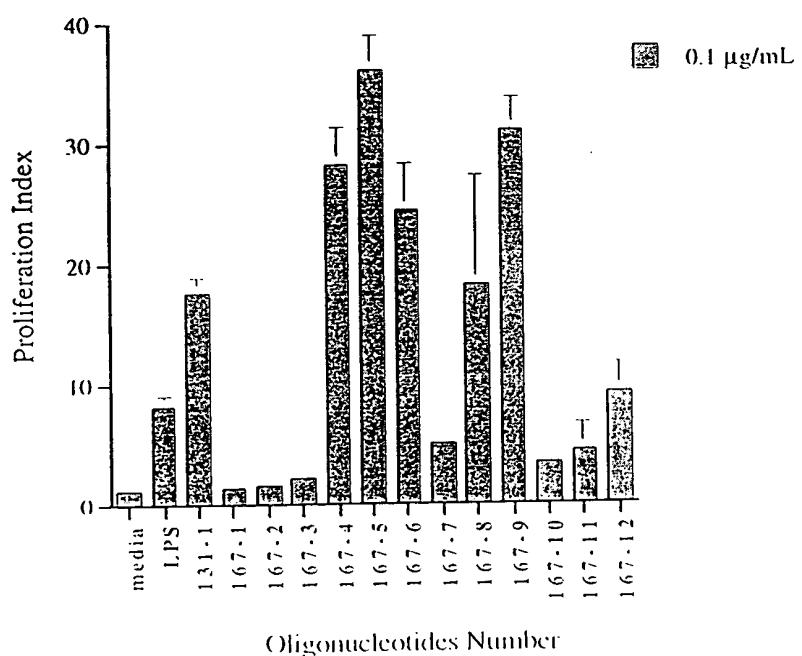


Figure 14 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification
131-1	5'-CTATCTGACGTTCTCTGT-3'
167-1	5'-CTATCTGXCGTTCTCTGT-3'
167-2	5'-CTATCTXACGTTCTCTGT-3'
167-3	5'-CTATCXGACGTTCTCTGT-3'
167-4	5'-CTATXTGACGTTCTCTGT-3'
167-5	5'-CTAXCTGACGTTCTCTGT-3'
167-6	5'-CTXXCTGACGTTCTCTGT-3'
167-7	5'-CTATCTGACGXCTCTGT-3'
167-8	5'-CTATCTGACGTXCTCTGT-3'
167-9	5'-CTATCTGACGTTXTCTGT-3'
167-10	5'-CTATCTGACGTTCXCTGT-3'
167-11	5'-CTATCTGACGTTCTXTGT-3'
167-12	5'-CTATCTGACGTTCTXXGT-3'

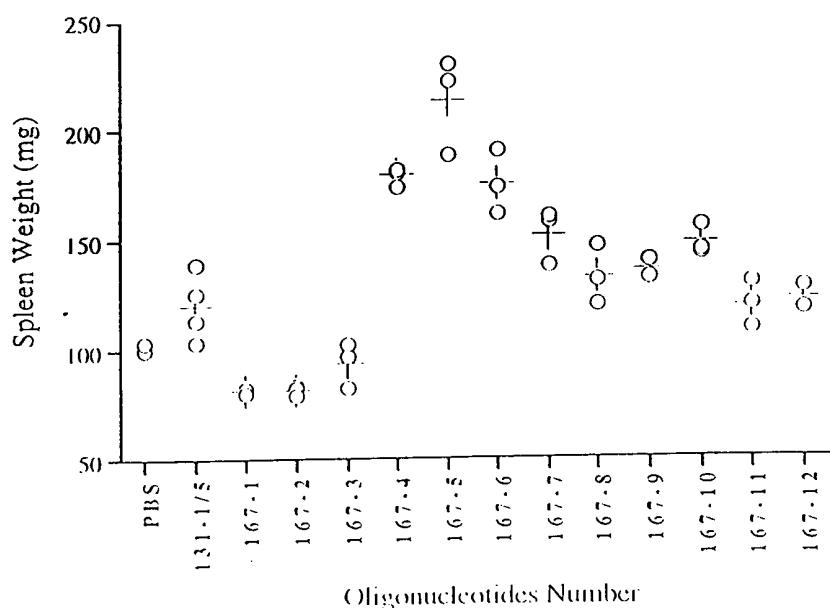
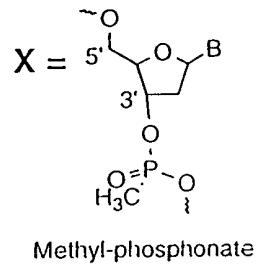
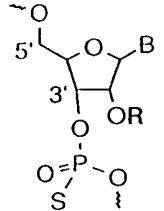


Figure 15 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification	
113-1	5'-TCCATGACGTTCCCTGATGC-3'	
23-1	5'-TCCATGXCGTTCCCTGATGC-3'	
23-3	5'-TCCAXGACGTTCCCTGATGC-3'	
29-2	5'-TYYATGACGGTCCTGATGC-3'	 $\text{R}_X = 2'\text{-O-Methylribonucleoside}$ $\text{R}_Y = 2'\text{-O-Methoxyethylribonucleoside}$

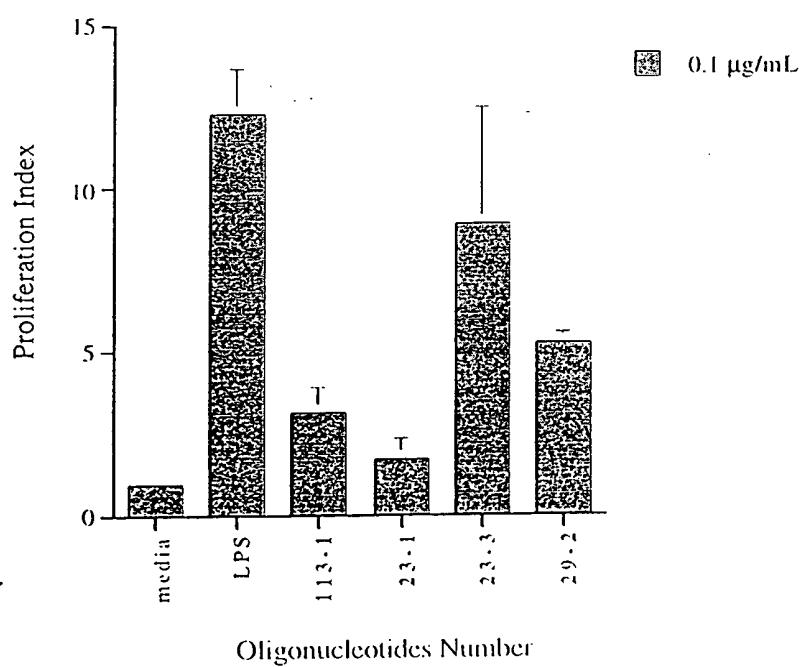
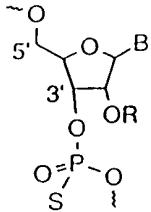


Figure 16 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification	
113-1	5'-TCCATGACGTTCCCTGATGC-3'	
23-1	5'-TCCATGXCAGTTCCCTGATGC-3'	
23-3	5'-TCCAXGACGTTCCCTGATGC-3'	
29-2	5'-TYYATGACGGTCCTGATGC-3'	 $R_x = 2'-O\text{-Methylribonucleoside}$ $R_y = 2'-O\text{-Methoxyethylribonucleoside}$

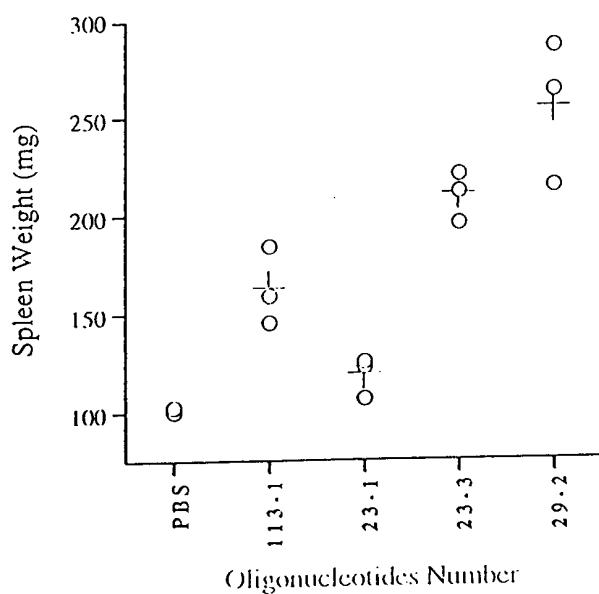


Figure 17 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification
1	5'-G A G A A C G C T C G A C C T T-3' ↑ ↑
2	5'-G A G A A C G C T C G A C C T T-3' —— 5'-G A G A A C G C T C G A C C T T-3' ↑ ↑ ↑ ↑
3	3'-T T C C A G C T C G C A A G A G-5' —— 5'-G A G A A C G C T C G A C C T T-3' ↑ ↑ ↑ ↑
4	5'-G A G A A C G C T C G A C C T T-3' —— 3'-T T C C A G C T C G C A A G A G-5' ↑ ↑ ↑ ↑
5	5'-T C T C C C A G C G T G C G C C A T-3' ↑
6	5'-T C C C A G C G T G C G C C A T-3' —— 5'-T C C C A G C G T G C G C C A T-3' ↑ ↑
7	3'-T A C C G C G T G C G A C C C T-5' —— 5'-T C C C A G C G T G C G C C A T-3' ↑ ↑
8	5'-T C C C A G C G T G C G C C A T-3' —— 3'-T A C C G C G T G C G A C C C T-5' ↑ ↑

The figure shows three chemical diagrams of phosphorothioate linkages.
 1. On the left, a 3'-5' linkage is shown where the 3' carbon of one deoxyribose sugar is linked to the 5' carbon of the adjacent sugar via a phosphorothioate group ($\text{O}=\text{P}(=\text{O})(\text{S}^{\ominus})\text{O}$).
 2. In the middle, a 5'-5' linkage is depicted where two 5' carbons are joined by a phosphorothioate bridge.
 3. On the right, a 3'-3' linkage is illustrated where the 3' carbon of one sugar is linked to the 3' carbon of another via a phosphorothioate group.

→ 5'-3'- direction of CpG motif

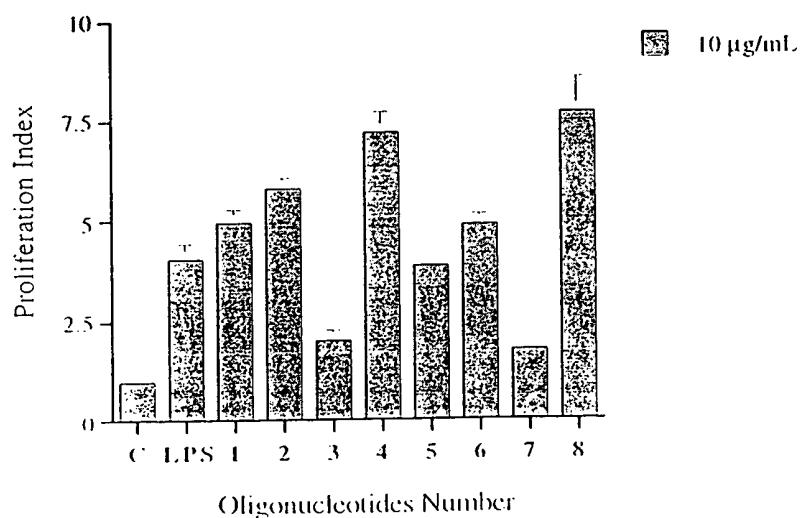


Figure 18 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification
131-1	5'-CTATCTGACGTTCTCTGT-3'
175-1	5'-CTATXTGACGTTCTCTGT-3'
175-2	5'-CTATCTGACGTTCTCTGT-3'
175-3	5'-CTAXXTGACGTTCTCTGT-3'
175-4	5'-CTATCTGACGTTCTCTGT-3'
175-5	5'-CTATCTGAXXTTCTCTGT-3'
175-6	5'-CTATCTXACGTTCTCTGT-3'
175-7	5'-CTATCTGACGTXCTCTGT-3'
175-9	5'-CTATCTGACGTTCTCTGT-3' (all- β -L-DNA/PS)

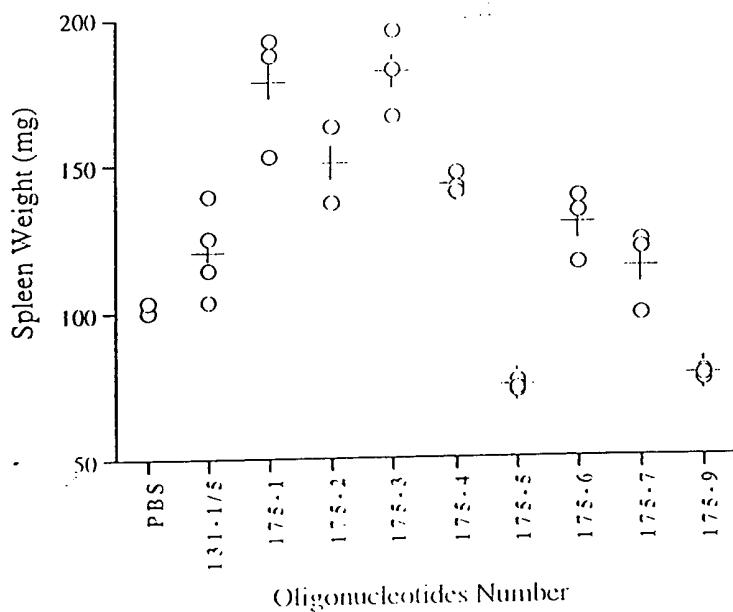
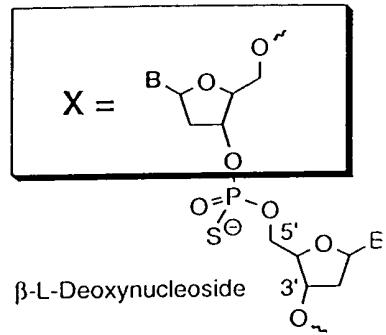
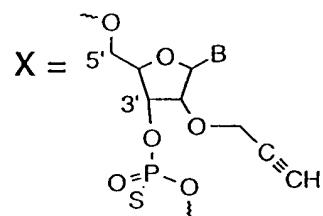


Figure 19 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification
131-1	5'-CTATCTGACGTTCTCTGT-3'
173-1	5'-CTATXTGACGTTCTCTGT-3'
173-2	5'-CTATCTGACGTTCTXTGT-3'



2'-O-Propargyl-ribonucleoside

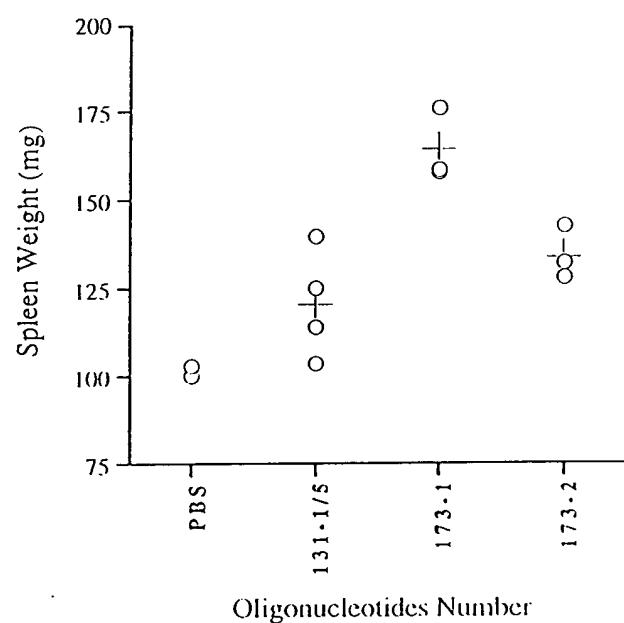


Figure 20 Oligodeoxynucleotide Phosphorothioates and Modification of Linkages

Oligo No.	Sequence & Modification
133-1	5'-CCTACTAGCGTTCTCATC-3'
143-1	5'-CCTXXTAGCGTTCTCATC-3'
143-2	5'-CCTYYTAGCGTTCTCATC-3'
143-3	5'-CCTZZTAGCGTTCTCATC-3'
143-4	5'-CCTXXTAGCGTVCTCATC-3'
143-5	5'-CCTACTAG <u>G</u> CTTCTCATC-3'

X = 1',2'-Dideoxyribose
 Y = C3-Linker
 Z = 3'-OMe
 V = 2'-OMe

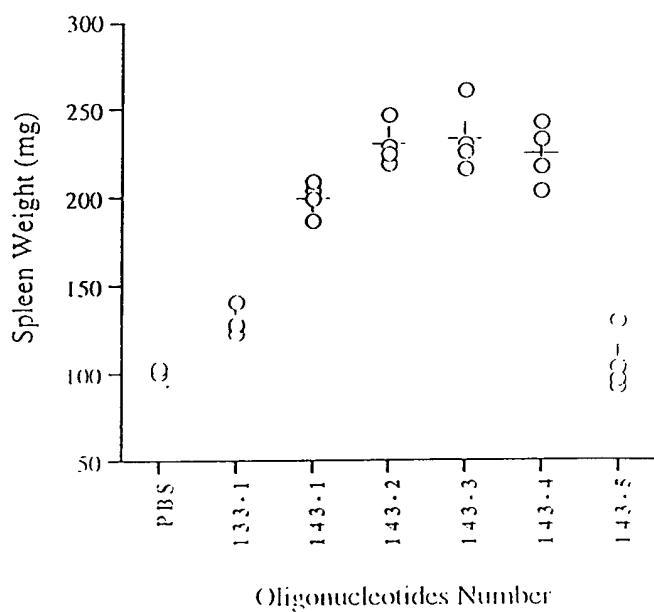


Figure 21 Oligodeoxynucleotide Phosphorothioates and Site of Modification

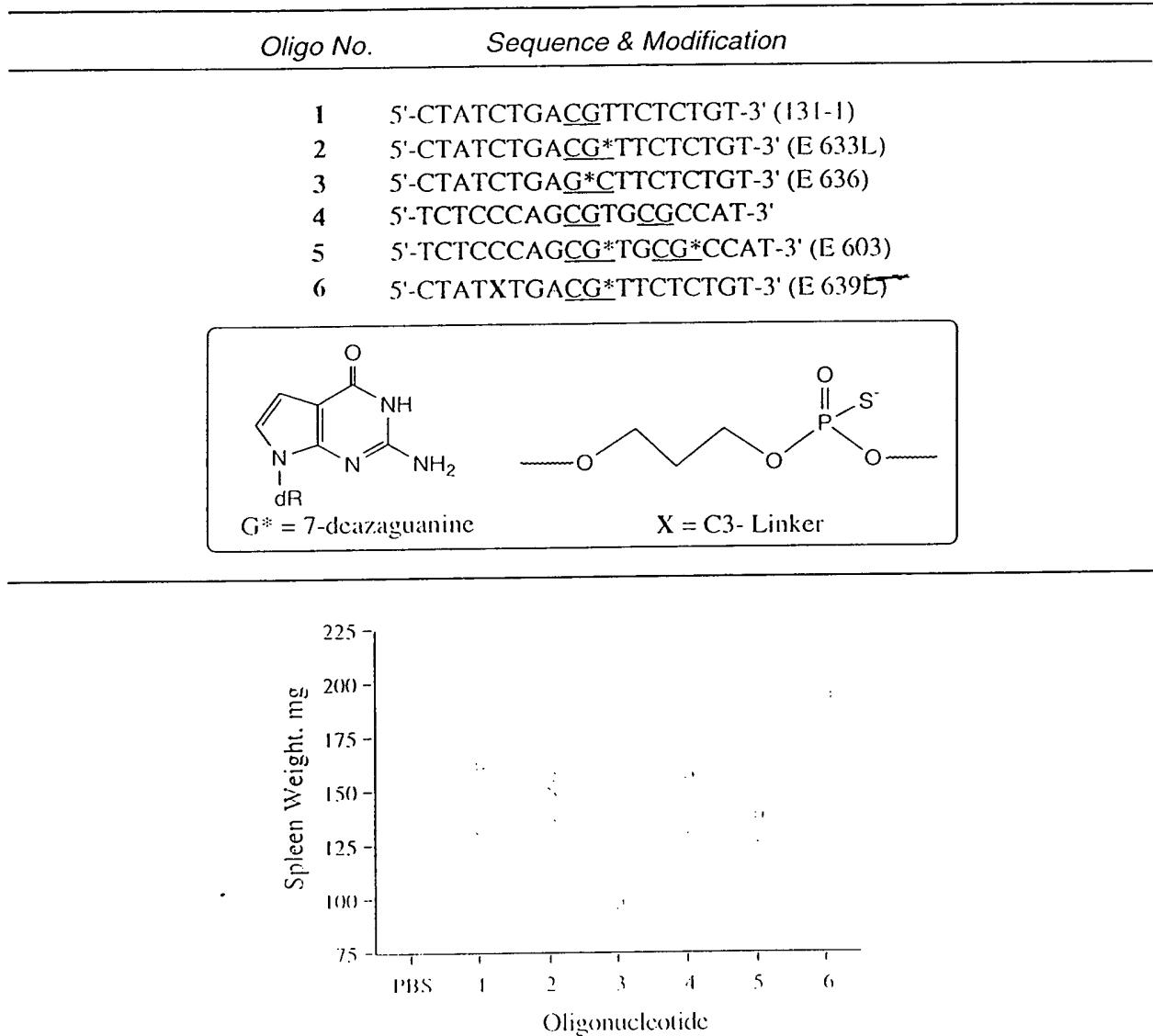


Figure 22 Oligodeoxynucleotide Phosphorothioates and Site of Modification

Oligo No.	Sequence & Modification
1	5'-CTATCTG <u>ACG</u> TTCTCTGT-3' (131-1)
2	5'-CTATCTG <u>ACG*</u> TTCTCTGT-3' (E 682)
3	5'-CTATCTG <u>GAG*</u> CTTCTCTGT-3' (E 683)

$\text{G}^{\ddagger} = 6\text{-thioguanine}$

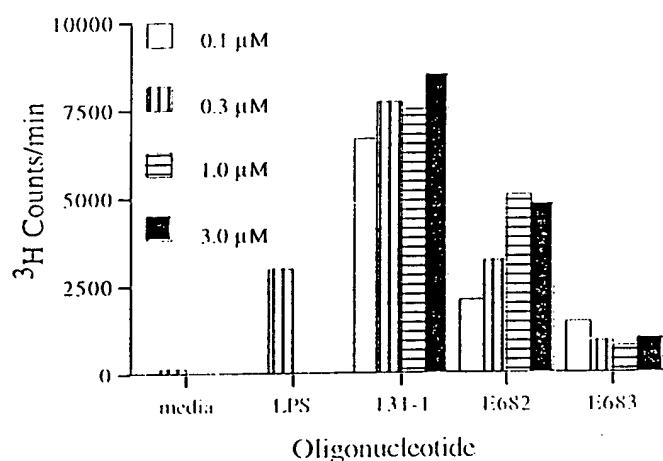


Figure 23 Oligodeoxynucleotide Phosphorothioates and Site of Modification

Oligo No.	Sequence & Modification
1	5'-CTATCTGAC <u>G</u> C <u>T</u> TCTCTGT-3'
2	5'-CTATCTGAC* <u>G</u> T <u>T</u> TCTCTGT-3'
3	5'-CTATCTGAC <u>C</u> <u>C</u> *T <u>T</u> TCTCTGT-3'
4	5'-CTATCTGAC** <u>G</u> T <u>T</u> TCTCTGT-3'
5	5'-CTATCTGAC <u>C</u> <u>C</u> **T <u>T</u> TCTCTGT-3'

Nc1nc(O)cnc1=O Nc1nc(CCC)ncnc1=O

C* = 5-hydroxy-cytosine C** = N4-ethyl-cytosine

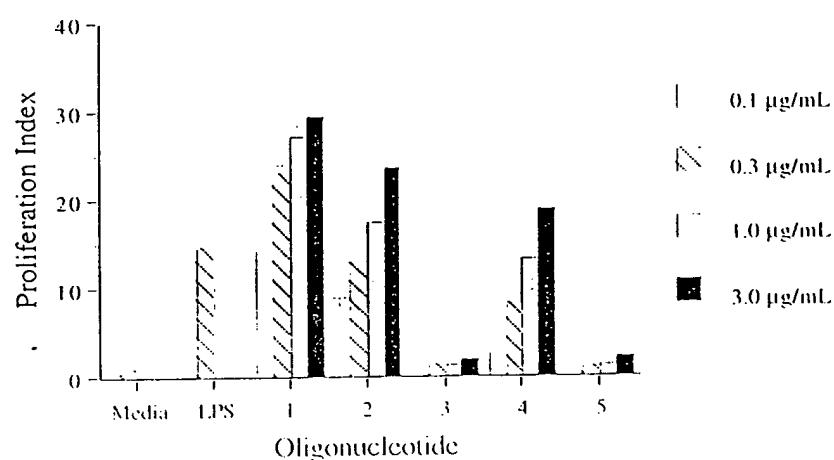


Figure 24 Oligodeoxynucleotide Phosphorothioates and Site of Modification

Oligo No.	Sequence & Modification
1	5'-CTATCTGAC <u>G</u> TTCTCTGT-3'
2	5'-CTATCTGAC <u>G</u> *GTTCTCTGT-3'
3	5'-CTATCTGAC <u>CC</u> *TTCTCTGT-3'
4	5'-CTATCTGAC <u>CC</u> **GTTCTCTGT-3'
5	5'-CTATCTGAC <u>CC</u> **TTCTCTGT-3'

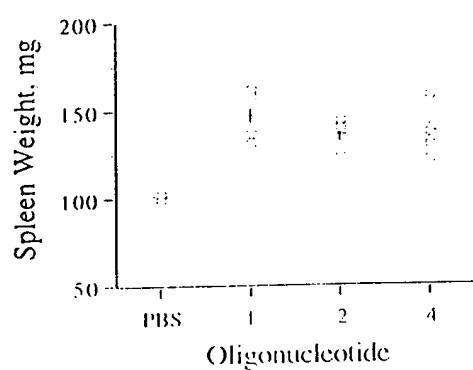
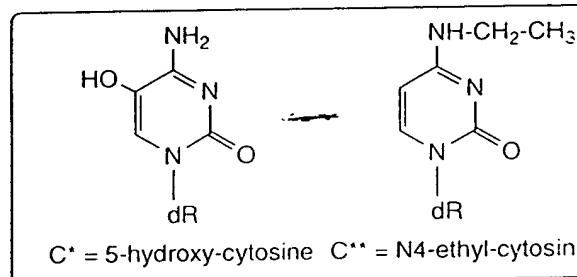


Figure 25 Oligodeoxynucleotide Phosphorothioates and Site of Modification

Oligo No.	Sequence & Modification
1	5'-CTATCTGAC <u>G</u> TTC <u>T</u> GT-3'
2	5'-CTATCTGAC <u>G</u> *GTT <u>T</u> CTGT-3'
3	5'-CTATCTGACC <u>G</u> *TT <u>T</u> CTGT-3'

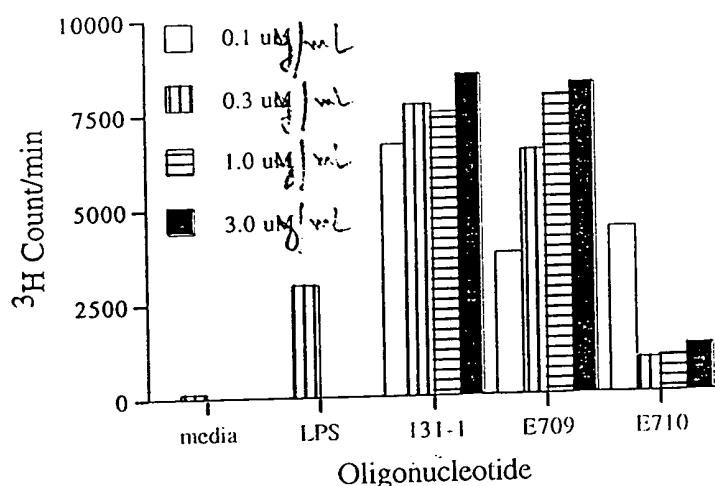
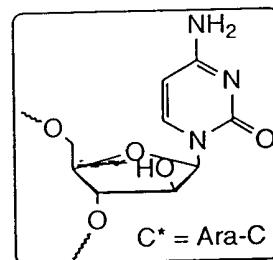


Figure 26 Oligodeoxynucleotide Phosphorothioates and Site of Modification

Oligo No. Sequence & Modification

- 1 5'-CTATCTGACGTTCTCTGT-3' (131-1)
- 2 5'-CTATCTGAC*GTTCTCTGT-3' (E 647)
- 3 5'-CTATXTGAC*GTTCTCTGT-3' (E 653)

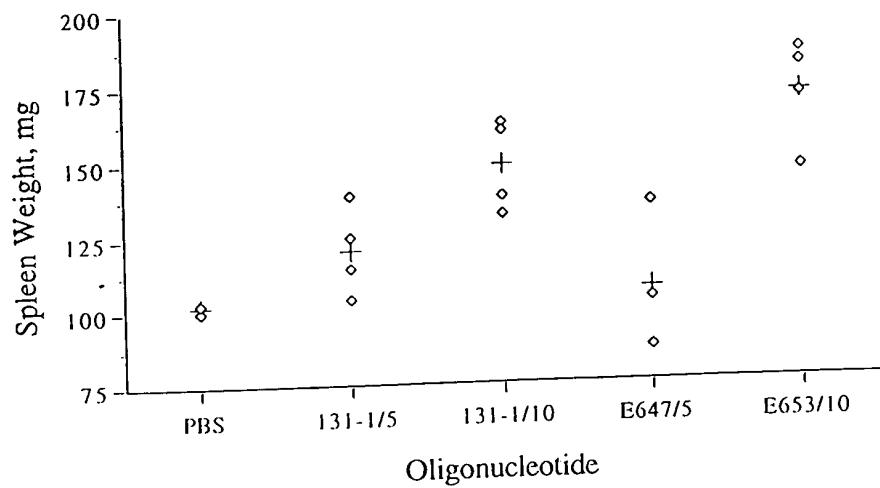
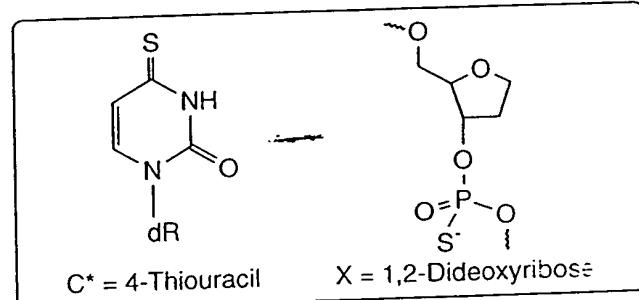


Figure 27

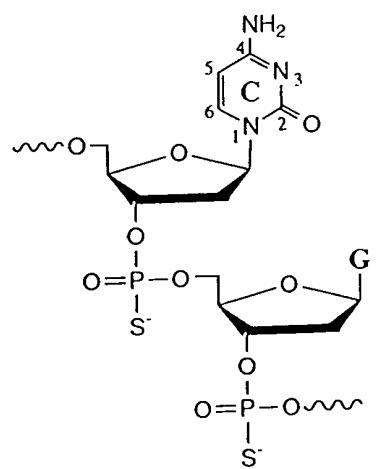


Figure 28

